

REMARKS

Reconsideration is requested.

Claims 1-67, 71-72, 75, 77-78, 80-84, 91-94 and 98-101 have been canceled, without prejudice. Claim 102 has been added and is similar to amended claim 70 but for the claim dependency. Claim 102 has been added so that subsequent dependent claims will be properly multiply dependent. The claims have been amended to advance prosecution without prejudice. Entry of the above amendments is requested to, at a minimum, place the application in better form for any future appeal by, at least, obviating the Section 112, first paragraph, rejection of claims 77 and 98-101, which have been canceled above.

Amended claims 68-70 and 102 are based on unamended claims 68-70 with the original recitation of recombinant vaccinia vectors and specifying that the 1st hydrophobic domain of E1 should be present. The boundary "285" is described in the application where the 1st hydrophobic domain is described as the domain of the envelope region between positions 264 to 293, plus or minus 8 amino acids (previous claim 70; lines 11-13 on page 18). To include the hydrophobic domain the envelope region should end at position 293, plus or minus 8 amino acids. Subtracting 8 from 293 yields 285. The boundary "285" thus is supported by the description. The boundary "326" is supported by line 11 on page 18 of the description. The recitation of lower eukaryotic or mammalian expression in claim 69 has been deleted due to the inclusion of the recitation of vaccinia vectors. Vectors comprising E1 with this deletion have been omitted from claims 95-97.

The Section 102 rejection of claims 70, 73, 76, 87 and 95-97 over Watanabe et al. (US Patent No. 5,610,009) will be moot upon entry of the above amendments. Entry of the above amendments and withdrawal of the Section 102 rejection over Watanabe are requested.

The Section 103 rejection of claims 68-70, 73-74, 76, 79, 87-88, 91 and 95-96 over Lanford (Virology 1993, Vol. 197, pp 225-235), Ralston (Journal of Virology 1993, Vol. 67, pp 6753-6761), Watanabe and Ford (Protein Expression and Purification 1991, Vol. 2, pp 95-107) is obviated by the above amendments. Reconsideration and withdrawal of the rejection are requested in view of the following distinguishing comments.

The deficiencies of Watanabe are noted above. The claims, directed to recombinant vaccinia vectors, are submitted to be distinguishable from Lanford et al. in combination with Ralston et al. Lanford et al. point to deficiencies of the E1a (117-386) and E1t (117-340) expressed in insect cells: "Other anomalies were observed in the processing of E1 in this study." (page 233, right-hand column, 2nd full paragraph). Lanford et al. also await "the development of more appropriate expression systems" (page 233, right-hand column, last sentence of 2nd full paragraph).

Ralston et al. are believed to merely disclose a number of recombinant vaccinia vectors for **co-expression of full-length Core AND part of E1** (1-304 and 1-381). The vectors of Ralston et al. thus serve a purpose other than the vectors of Lanford et al.

Even if one were to combine Lanford et al. and Ralston et al., which the applicants do not believe one would have been motivated by the art to do, one would obtain, at best, one of the two following possibilities:

- the development of **baculovirus** vectors expressing Core **and** part of E1 (incorporating Ralston et al. into Lanford et al.), or
- the development of **vaccinia** vectors expressing **anything but** E1 in the regions 117-386 and 117-340 (incorporating Lanford et al. into Ralston et al.) as the occurrence of the reported anomalies is expected.

Either of these two combinations is, if teaching anything, teaching clearly away from the presently claimed invention.

The teachings of Watanabe and/or Ford in combination with Lanford and Ralston do not alter this conclusion.

In addition, the recombinant vectors of the current invention provide unexpected properties, as disclosed in De Martynoff et al. (Viral Hepatitis and liver disease. Proceedings of IX international symposium on viral hepatitis and liver disease. Rome, Italy, 21-25 April 1996. Edizioni Minerva Medica, Turin 1997, a copy of which was supplied with the Submission of June 7, 2004). Firstly the Examiner is referred to Table 1 of the present invention (pages 63-64) wherein recombinant vaccinia plasmids and viruses are listed, e.g., pvHCV-11A and pvHCV-10A (4th and 6th plasmid, respectively, in Table 1). Secondly, from Example 2.5 (pages 44-45) it is clear that recombinant vaccinia viruses are named according to the vaccinia recombinant plasmid. Recombinant viruses vvHCV-11A and vvHCV-10A are for example obtained from recombination with plasmids pvHCV-11A and pvHCV-10A, respectively. Referring back to Table 1, the codes of the recombinant vaccinia viruses can thus be easily obtained by exchanging "pv" in the plasmid name for "vv". Nearly all of the recombinant vaccinia viruses schematically provided in Figure 1 on page 220 of De Martynoff et al. (1997) are

the same as the ones listed in Table 1 of the present invention. In particular, vvHCV-11A and vvHCV-10A of the current invention are the same as vvHCV-11A and vvHCV-10A listed as the 7th and 9th recombinant vaccinia viruses in Figure 1 of De Martynoff et al. (1997).

De Martynoff et al. (1997) further states in the last sentence of the third paragraph of the left-hand column of page 221:

"In contrast with constructs encoding single envelope proteins (vvHCV-11A, -10A, -44, Fig.2, lanes 4, 5, 6 and 8), expression levels decreased along with carboxyterminal position of E1 or E2 in polyprotein constructs (vvHCV-33, -65, -66; lanes 3, 8 and 9)."

This illustrates that defining the construct for E1 expression as containing the termination points as presently claimed (claims 68 and 69) provides the advantage of increasing E1 expression levels. This is not taught or suggested by Lanford et al., Ralston et al., Watanabe and/or Ford.

The claims are submitted to be patentable over the cited art. Entry of the above amendments and withdrawal of the Section 103 rejection are requested.

The Section 112, first paragraph, rejection of claims 77 and 98-101 will be moot upon entry of the above amendments. Entry of the amendments is requested.

The Section 112, second paragraph, rejection of claims 95-97 is obviated by the above amendments. Reconsideration and withdrawal of the rejection are requested in view of the above and the following comments.

One of ordinary skill in the art will appreciate from the present specification that a "hepatitis C virus single envelope protein" of the invention defines a polyprotein of at

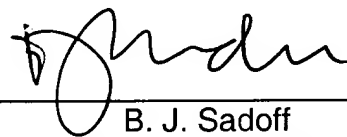
least one HCV epitope of either the E1 or the E2 region. See, page 3, lines 32-34 of the specification. Epitopes are defined in the specification as containing at least 3 or more amino acids. See, page 4, lines 5-8 and page 10, lines 22-34 of the specification. The vectors of the disclosed and claimed invention are described in the specification at, for example, page 17, lines 14-25, as allowing expression of a "single....E1 of the invention." The applicants submit that "parts thereof" and "an epitope encoding part thereof" will be appreciated, in view of the specification, to require a nucleic acid sequence which encodes more than "one amino acid residue" as suggested by the Examiner on page 6 of the June 30, 2004 Office Action. Entry of the above amendments and withdrawal of the Section 112, second paragraph, rejection are requested.

The claims are submitted to be in condition for allowance and a Notice to that effect is requested.

Respectfully submitted,

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By: _____



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